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Board of Registration in Pharmacy

Advisory: Non-Sterile Compounding

In addition to the requirements of MGL, 247 CMR, USP <795>, and <800>, the Board of Registration in Pharmacy ("Board") would like to provide a review of select requirements and guidance for the practice of non-sterile compounding by Board licensed pharmacies.

In accordance with MGL c.112 section 39D, **complex non-sterile compounding** is specifically defined with certain requirements, including additional specialty licensure (see Section VII below).

I. Definitions

a. **Non-sterile compounding** is defined as the process of combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug or bulk drug substance to create a non-sterile preparation (adapted from the latest draft of USP <795>).

b. **Complex non-sterile compounding** is defined as the compounding of drug preparations which require special training, a special environment or special facilities or equipment or the use of compounding techniques and procedures that may present an elevated risk to the compounder or the patient (MGL c.112 section 39D). See section VII (b) below for examples.

Note: The Board considers the compounding of NIOSH drug containing preparations or other hazardous agents to be complex non-sterile compounding.

II. General

a. Pharmacies must have policies and procedures covering all aspects of non-sterile compounding, including training, based on the type of the compounding performed.
b. Patient specific prescriptions are required to dispense any compounded preparation into or from Massachusetts.
c. Copies of commercially available, FDA approved drugs or drug preparations may not be compounded except to meet the unique medical need of an individual patient by producing a significant difference between the compounded drug preparation and a comparable commercially available drug whether it is for human or animal use. See policy: https://www.mass.gov/doc/policy-2020-02-compounding-of-commercially-available-drugs/download
d. Pharmacies may provide emergency kits ("e-kit") containing limited quantities of Schedule VI compounded medications to a licensed veterinarian for the purpose of direct administration or dispensing in emergency situations in accordance with Board policy: https://www.mass.gov/doc/joint-policy-2019-06-compounded-emergency-medications-for-veterinarian-use/download
e. Pharmacies may participate in research drug studies with compounded medications in accordance with Board policy: https://www.mass.gov/doc/2018-06-retail-pharmacy-participation-in-investigational-drug-studies/download

III. Non-Sterile Compounding Process

a. A pharmacy must follow a master formulation record (i.e. formulation sheet) each time it prepares a compounded non-sterile preparation. The master formulations must be based on USP standards as well as any relevant scientific data and / or direct validation testing, as applicable.
b. Simple reconstitution of commercially available FDA approved drug preparations in accordance with manufacturer package insert instructions is not considered compounding.
c. Breaking or splitting drugs is not considered compounding, but for hazardous drugs, USP <800> must be followed to perform these activities. See advisory: https://www.mass.gov/doc/implementation-of-usp-in-community-pharmacies-0/download

d. Pre-measured compounding kits are still considered compounding and all relevant USP standards must be followed.
e. Active Pharmaceutical Ingredients ("API") and other bulk powders must be obtained from a facility that is registered by the FDA.

Note: The Board would like to remind non-sterile compounders to exercise extreme caution in assuring proper dosages when compounding with API powders by verifying if the API is a pure powder or a trituration (dilution).

IV. Facility and Equipment

a. Pharmacies must have a designated compounding area that should be at least 10 square feet of counter space. This area should be separated or otherwise protected from water sources (i.e., sink).
b. Surfaces in compounding areas should be smooth, seamless, impervious, free from cracks and crevices, and non-shedding to facilitate cleaning. Note: Carpeting is not allowed in the compounding space per the latest draft of USP <795>.
c. Compounding facilities must be maintained in a clean and sanitary manner including sinks, utensils, and equipment. Review the FDA's Insanitary Conditions at Compounding Facilities guidance document.
d. Equipment used for compounding must be in a good state of repair and properly maintained.
e. Scales / balances must be properly maintained and sealed at least once per calendar year. See newsletter for details: https://nabp.pharmacy/wp-content/uploads/2016/06/Massachusetts-Newsletter-November-2019.pdf
f. Space, equipment, and materials should be designed, arranged, and used in a way that minimizes errors and cross-contamination.
g. Before beginning any renovations, retail pharmacies must apply for approval using this form: https://www.mass.gov/how-to/request-approval-for-a-pharmacy-renovation-or-expansion

V. Labeling / BUDs

a. Beyond use dates ("BUD") must be assigned in accordance with USP <795> or a validated formula. Assure that BUDs are appropriately assigned in the pharmacy's computer system and are not defaulted to one year.

b. In addition to standard prescription labeling, a statement that the drug is a non-sterile compounded drug preparation must also be included (MGL c. 94C section 21).

VI. Documentation

a. A reconstitution log (or similar documentation) for the preparation of commercially available products (e.g., antibiotic suspensions, erythromycin-benzoyl peroxide gel, etc.) is recommended.
b. Flavoring agents added to commercially available products must be documented as part of the prescription record, reconstitution log, or other similar documentation.
c. Each compounded non-sterile preparation must be documented on a compounding record (i.e. compounding log).
   Note: The compounding record serves as the accountability documentation as required by MGL c.112 section 39D.
d. All pharmacies are required to maintain a defective drug log for any compounded drug preparation that is or may be defective. See advisory for details:
   https://www.mass.gov/advisory/advisory-on-pharmacy-requirement-to-maintain-defective-drug-preparation-log

VII. Complex Non-Sterile Compounding

a. An additional pharmacy specialty license will be required to prepare complex non-sterile preparations:
   https://www.mass.gov/pharmacy-licensing
b. The Board considers the following to be examples of complex non-sterile compounding (not all inclusive):
   i. compounding of NIOSH drug containing preparations or other hazardous agents;
   ii. use of complex calculations such as accounting for loss on drying, salt conversions, multiple aliquots, etc.; and
   iii. preparation of the following dosage forms:
      1. transdermal dosage forms
      2. capsules
      3. suppositories
      4. troches
      5. lollipops
      6. sublingual dosage forms

7. tablets
8. tablet triturates
9. modified-release preparations
10. other dosage forms intended to deliver systemic effects (inserts, nasal sprays, nasal irrigations, certain gels, etc.)

c. Additional requirements for pharmacies engaged in complex non-sterile compounding:
   i. a dedicated compounding room with a containment hood(s) is recommended for complex non-sterile compounding but is required for hazardous drug (HD) compounding (i.e. containment secondary engineering control with containment primary engineering control);
   ii. HD and non-HD non-sterile compounding cannot occur in the same room or primary engineering control. A separate room with a separate containment hood(s) is required for HD compounding (per USP <800>);
   iii. compounding of non-sterile preparations using bulk drug substances must comply with FDA's guidance "Bulk Drug Substances Used in Compounding Under Section 503A of the FD&C Act"; bulk drug substances must be accompanied by a valid certificate of analysis;
   iv. pharmacists engaged in complex non-sterile compounding must obtain 3 continuing education hours in complex non-sterile compounding each calendar year;
   v. repairs and / or service of complex non-sterile compounding facilities must be conducted in accordance with the Board's advisory: https://www.mass.gov/doc/advisory-on-conducting-repairs-or-service-to-sterile-compounding-facilities-or-facilities/download;
   vi. retail complex non-sterile compounding pharmacies licensed by the Board are required to report volume and distribution data each calendar year.

Please direct any questions to: **Pharmacy.Admin@mass.gov**